

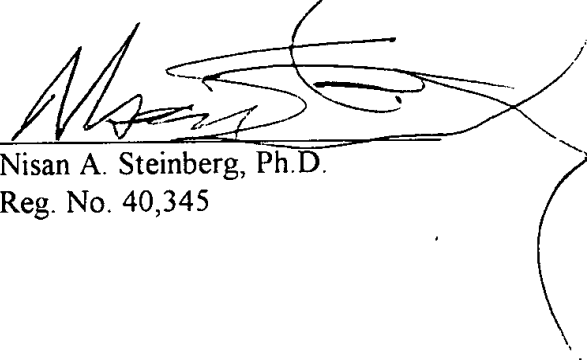
Applicant has herein canceled Claims 1, 4, 9-10, and 17-21, as being directed to a non-elected group and has amended Claims 1, 5, 11, and 25, in accordance with Applicant's election, to remove the recitation of "neural progenitor cells", "neuronal cells", and signal molecules and markers inapplicable to glial cells, as being directed to non-elected subject matter. Although Claim 9 (canceled) recites GFAP and O4, which are directed to elected subject matter, Applicant considers Claim 9 to be redundant in view of the limitations of Claim 1, step (e).

Additional amendments in Claim 1 (deleting "any of") and Claim 11 (changing lower case "a"- "c" with upper case letters to comport with Claim 12) are merely cosmetic changes made for the sake of greater clarity.

Applicant's election is made with a complete reservation of all rights under 35 U.S.C. § 121.

Respectfully submitted,

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**Version with Markings to Show Changes Made**

**In the Claims:**

Please cancel Claims 4, 7, 9, 10, and 17-21, without prejudice. Please amend Claims 1, 5, 11, and 25 as follows.

1. (Thrice Amended) An in vitro method of transdifferentiating an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell, comprising:

(a) culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s), said cell(s) derived from the skin of a mammalian subject;

(b) transfecting said epidermal basal cell, in vitro, with one or more eukaryotic expression vector(s) containing at least one cDNA encoding a human neurogenic transcription factor, or homologous non-human counterpart, or active fragment(s) thereof, selected from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, such that at least one of the neurogenic transcription factor(s) is expressed in said cell;

(c) growing the transfected cell in the presence of at least one antisense oligonucleotide comprising a segment of a human MSX1 gene and/or human HES1 gene, or homologous non-human counterpart of either of these, in an amount sufficient to suppress the expression of functional MSX1 gene product and/or HES1 gene product;

(d) growing said epidermal cell with a retinoid and at least one signal molecule selected from the group consisting of [BDNF, JCNTF, [PDGF, NGF, NT-3, NT-4,] sonic hedgehog, [and] sonic hedgehog aminoterminal peptide, [or a cytokine comprising] and IL-6, whereby the cell is transdifferentiated into a cell having one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell; and

(e) wherein the physiological and/or immunological feature is expression of a marker selected from the group consisting of [nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific  $\beta$ -tubulin, neural-specific enolase, microtubule associated

protein 2,] glial fibrillary acidic protein (GFAP)[,] and O4, or a combination of [any of] these.

2. (Reiterated) The method of Claim 1, wherein the eukaryotic expression vector(s) of the transfection step comprise a CMV promoter sequence operatively linked to a DNA(s) encoding the neurogenic transcription factor selected from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, and wherein the DNA encoding the neurogenic transcription factor is of human origin or is a homologous non-human counterpart, or is an active fragment of a gene encoding any of these.

Claim 4 is canceled.

5. (Twice Amended) A transdifferentiated cell having one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell, comprising:

an epidermal basal cell transfected with one or more expression vectors comprising a CMV promoter sequence operatively linked to a DNA(s) encoding the neurogenic transcription factor NeuroD1, NeuroD2, ASH1, Zic1, Zic3, or MyT1, wherein the DNA encoding the neurogenic transcription factor is of human origin, or is a non-human homologous counterpart, or is an active fragment of a gene encoding any of these, said cell being treated with at least one antisense oligonucleotide comprising a segment(s) of human MSX1 gene or human HES1 gene, or non-human homologous counterpart thereof, and wherein said cell was grown in the presence of a retinoid and at least one signal molecule selected from the group consisting of [BDNF,] CNTF,[ NGF, NT-3, NT-4,] IL-6, sonic hedgehog, and sonic hedgehog aminoterminal peptide, thereby transdifferentiating said epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell said cell expressing at least one marker selected from the group consisting of [nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific  $\beta$ -tubulin, neural-specific enolase, microtubule associated protein 2,] glial fibrillary acidic protein (GFAP)[,] and O4, or a

combination of [any of] these.

Claim 7 is canceled.

8. (Reiterated) A transdifferentiated cell produced by the process of Claim 1.

Claims 9 and 10 are canceled.

11. (Twice Amended) A kit for converting, in vitro, epidermal basal cells into cells having one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell, said kit comprising:

    ([a]A) one or more eukaryotic expression vector(s) containing cDNA encoding a neurogenic transcription factor, or fragment thereof, from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, or a non-human homologous counterpart of any of these;

    ([b]B) at least one antisense oligonucleotide corresponding to the human MSX1 gene, the human HES1 gene, or a non-human homologous counterpart of either of these; and

    ([c]C) a retinoid and at least one signal molecule selected from the group consisting of [BDNF,] CNTF, [PDGF, NGF, NT-3, NT-4,] sonic hedgehog, and sonic hedgehog aminoterminal peptide.

12. (Reiterated) The kit of Claim 11, further comprising instructions for using (A), (B), and (C) in transdifferentiating a mammalian subject's epidermal basal cell(s).

16. (Reiterated) The transdifferentiated cell of Claim 8, wherein the cell further displays the physiological feature of a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

Claims 17-21 are canceled.

22. (Reiterated) The transdifferentiated cell of Claim 8, wherein the cell is of human origin.

23. (Reiterated) The cell of Claim 8, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

24. (Reiterated) The transdifferentiated cell of Claim 23, wherein the physiological and/or immunological feature is expression of glial fibrillary acidic protein (GFAP) or O4.

25. (Twice Amended) An in vitro cell culture derived from the transdifferentiated cell of Claim 8, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a [neural progenitor, neuronal, or] glial cell.

26. (Reiterated) The method of Claim 1, wherein culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s) comprises separating basal cells from keratinocytes using a calcium-free medium.

27. (Reiterated) The method of Claim 1, wherein said antisense oligonucleotide(s) is modified with one or more thio groups.